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LETTER TO THE EDITOR

Reversible dasatinib-related pulmonary arterial hypertension diagnosed by noninvasive echocardiography

To the Editor,

Pulmonary arterial hypertension (PAH) is an uncommon adverse effect of tyrosine kinase inhibitor. The article by Montani et al. [1] demonstrated PAH in patients treated with dasatinib. We report a 33-year-old male with chronic myeloid leukemia who suffered from shortness of breath after using dasatinib for 63 months. Noninvasive echocardiographic assessment revealed reversible PAH corresponding to clinical manifestations.

In October 2013, the patient presented with progressive dyspnea on exertion. He was known to have chronic phase chronic myeloid leukemia since January 1998. The initial laboratory data revealed eosinophilia, basophilia, low leukocyte alkaline phosphatase score, and positive BCR-ABL gene. He was initially treated with hydroxyurea 1000 mg twice per day, and then commenced imatinib at 800 mg/day since May 2002.

Under imatinib use, hematological complete remission was achieved, but there was no cytogenetic remission with a positive b2a2 BCR-ABL mutation. Point mutation in the kinase domain of BCR-ABL with F359V was identified. Imatinib was shifted to dasatinib 100 mg/day in July 2008 and a major molecular response was achieved. However, the patient suffered from progressive dyspnea in October 2013. The auscultation showed bilateral clear breathing sound. Prominence of bilateral hilar shadows were present on chest plain film (Fig. 1A). No thromboembolism evidence existed but dilatation of pulmonary trunk and proximal arteries in the chest computed tomography scan was found (Fig. 1B). Tc-99m DTPA (Diethylenetriamine pentaacetate) aerosol ventilation and Tc-99m MMA (microaggregated albulin) perfusion scintigraphy revealed a V (ventilation)/Q (perfusion) match reduction of the pulmonary functional volume. Doppler transthoracic echocardiography showed severe pulmonary arterial hypertension with an estimated pulmonary artery systolic pressure (PASP) of 105 mmHg, right atrial and right ventricular dilatation, and severe tricuspid regurgitation (Fig. 1C and D). We stopped using dasatinib but the symptoms persisted. One month later, we added on phosphodiesterase type 5 (PDE 5) inhibitor, sildenafil, and the symptoms improved gradually. Echocardiography was followed 3months later and estimated PASP regressed back to 45 mmHg (Fig. 1E). Dasatinib was replaced by nilotinib in this patient.

Pulmonary arterial hypertension (PAH) is defined as the mean pulmonary artery pressure (PAP) of >25 mmHg at rest, or >30 mmHg during exercise [2]. The definite diagnosis includes invasive right heart catheterization. However, there is a good correlation between transthoracic echocardiography and right heart catheterization measurement of PASP [3]. PAH is suspected if noninvasive PASP, determined by tricuspid regurgitation peak gradient (TRPG) and right atrial pressure(RAP) according to the simplified Bernoulli equation, is >35 mmHg measured by Doppler transthoracic echocardiography [2].

In 2007, a study by Quintás-Cardama et al. [4] suggested the association between dasatinib and pulmonary hypertension. In 2012, nine cases of symptomatic pulmonary hypertension treated with dasatinib have been identified definitely [1]. PAH appears as a late complication of dasatinib, occurring after 8–48 months of exposure [5]. The possible mechanism is dasatinib served as multi tyrosine kinase inhibitors, including BCR-ABL, SRC, c-kit, and PDGFR [5]. Symptoms are improved after discontinuation of dasatinib in the majority of cases, but some cases require PAH-specific therapy with sildenafil [5]. In summary, we reported a typical case of dasatinib-induced PAH diagnosed by noninvasive echocardiography.

Conflicts of interest: All authors declare no conflicts of interest.

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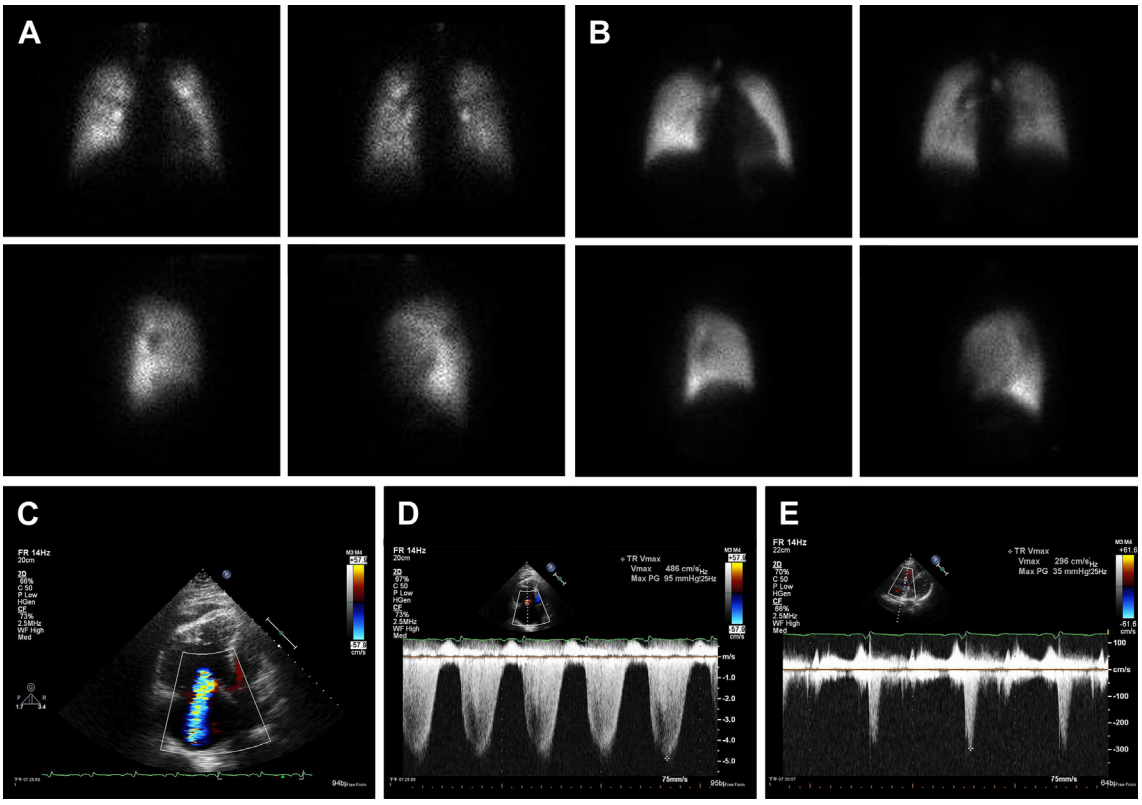

Figure 1. Characteristic image findings of reversible dasatinib-related pulmonary arterial hypertension. (A and B) Tc-99m DTPA (diethylenetriamine pentaacetate) aerosol ventilation and Tc-99m MMA (microaggregated albulin) perfusion scintigraphy reveals V (ventilation)/Q (perfusion) match reduction of pulmonary functional volume; (C and D) Doppler transthoracic echocardiography shows severe pulmonary arterial hypertension with estimated PASP 105 mmHg; (E); after stopping dasatinib and adding sildenafil, the estimated PASP fell back to 45 mmHg. PASP = pulmonary artery systolic pressure.

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